#### PATENT COOPERATION TREATY

	From the INTERNATIONAL BUREAU		
PCT	To:		
NOTIFICATION OF ELECTION  (PCT Rule 61.2)  Date of mailing (day/month/year)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE		
18 May 2000 (18.05.00)			
International application No. PCT/US98/08716	Applicant's or agent's file reference 00246/222WO1		
International filing date (day/month/year) 30 April 1998 (30.04.98)	Priority date (day/month/year)		
Applicant			
McMAHON, Andrew, P. et al			
in a notice effecting later election filed with the Inte	ry Examining Authority on: r 1999 (24.11.99)		
The International Bureau of WIPO 34, chemin des Colombettes	Authorized officer		
1211 Geneva 20, Switzerland	Claudio Borton		
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38		

#### Copy for the Elected Office (EO/US)

#### PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU		
PCT	То:	
NOTIFICATION OF THE RECORDING OF A CHANGE  (PCT Rule 92bis.1 and Administrative Instructions, Section 422)  Date of mailing (day/month/year) 23 August 2000 (23.08.00)	BEATTIE, Ingrid, A. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC One Financial Center Boston, MA 02111 ETATS-UNIS D'AMERIQUE	
Applicant's or agent's file reference	IMPORTANT NOTIFICATION	
00246/222WO1	IIII GITTART NOTE IO	
International application No. PCT/US98/08716	International filing date (day/month/year) 30 April 1998 (30.04.98)	
The following indications appeared on record concerning:     the applicant the inventor	X the agent the common representative	
Name and Address	State of Nationality State of Residence	
FREEMAN, John, W. Fish & Richardson P.C. 225 Franklin Street Boston, MA 02110-2804 United States of America	Telephone No. 617-542-5070 Facsimile No. 617-542-8906	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that t  X the person X the name X the add		
Name and Address	State of Nationality State of Residence	
BEATTIE, Ingrid, A. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC One Financial Center Boston, MA 02111 United States of America	Telephone No. 617-542-6000 Facsimile No.	
Officed States of Afficilea	617-542-2241	
	Tele innter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
X the receiving Office	the designated Offices concerned	
the International Searching Authority	X the elected Offices concerned	
X the International Preliminary Examining Authority	other:	
	Authorized officer	
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	I. Britel	
F	T   1   N   141   221   220   220   220	

#### PATENT COOPERATION TREATY

To: JOHN W. FREEMAN FISH & RICHARDSON P.C. 225 FRANKLIN STREET	_	CT
225 FRANKLIN STREET BOSTON, MASSACHUSETTS 02110-289/ECE LACK OF UNITY 9/15/198 SEP 03/ RESP TO SCARCING 9/13/19/18/18/18/18/18/18/18/18/18/18/18/18/18/	NOTIFICATION OF THE INTERNATION OR THE I	OF TRANSMITTAL OF DNAL SEARCH REPORT DECLARATION
Resp to scarch Rept 10/3/19818H & AICHAD	(PCI	「 Rule 44.1)
RESP TO SCATCHREDT TOBILIFISH & RICHARDS  ADSTRACT 91301988H & RICHARDS  ADDITION OF A PROPERTY THE PETERSE	Classing (date month/year) 81	AUG 1998
Applicants or agents file reference 00246/222WO1	FOR FURTHER ACTION	See paragraphs 1 and 4 below
International application No. PCT/US98/08716	International filing date (day/month/year) 04 MAY 1	998
Applicant PRESIDENT AND FELLOWS OF HARVARD COLLEGE		
1. X The applicant is hereby notified that the internationa  Filing of amendments and statement under Artic The applicant is entitled, if he so wishes, to amend When? The time limit for filing such amendm international search report; however, for Where? Directly to the International Bureau of V 34, chemin des Colombe	le 19: the claims of the international a tents is normally 2 months fro more details, see the notes on to VIPO	pplication (see Rule 46): om the date of transmittal of the the accompanying sheet.
1211 Geneva 20, Switze Facsimile No.: (41-22) 7	rland WORD 13	1 00 - Liling Sacramary
For more detailed instructions, see the notes or	the accompanying sheet.	
2. The applicant is hereby notified that no international Article 17(2)(a) to that effect is transmitted herewith		ned and that the declaration under
3. With regard to the protest against payment of (an the protest together with the decision thereon applicant's request to forward the texts of bot	has been transmitted to the Inter	mational Bureau together with the
no decision has been made yet on the protest		
4. Further action(s): The applicant is reminded of the fo	llowing:	
Shortly after 18 months from the priority date, the international the applicant wishes to avoid or postpone publication priority claim, must reach the International Bureau as completion of the technical preparations for internation	, a notice of withdrawal of the provided in rules 90 bis 1 and	international application, or of the
Within 19 months from the priority date, a demand for in wishes to postpone the entry into the national phase u		
Within 20 months from the priority date, the applicant mus all designated Offices which have not been elected in t date or could not be elected because they are not bou	t perform the prescribed acts for he demand or in a later election	entry into the national phase before
Name and mailing address of the ISA/US	Authorized officer	

ROBERT C. HAYES, PH.D.

(703) 308-0196

Telephone No.

Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231

Facsimile No. (703) 305-3230

#### PATENT COOPERATION TREATY

# **PCT**

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 00246/222WO1	FOR FURTHER see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year) (Earliest) Priority Date
PCT/US98/08716	04 MAY 1998 NONE
Applicant PRESIDENT AND FELLOWS OF	HARVARD COLLEGE
	been prepared by this International Searching Authority and is transmitted to the applicant being transmitted to the International Bureau.
This international search report co	isists of a total of $\frac{5}{2}$ sheets.
X It is also accompanied b	y a copy of each prior art document cited in this report.
1. Certain claims were fo	und unsearchable (See Box 1).
2. X Unity of invention is la	cking (See Box II).
	ation contains disclosure of a nucleotide and/or amino acid sequence listing and the carried out on the basis of the sequence listing
[	filed with the international application.
· · ·	furnished by the applicant separately from the international application,
<u> </u>	but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
	transcribed by this Authority.
4. With regard to the title, X	the text is approved as submitted by the applicant.
	the text has been established by this Authority to read as follows:
5. With regard to the abstract,	<b>.</b>
	the text is approved as submitted by the applicant.
[>	the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to	be published with the abstract is:
Figure No.	as suggested by the applicant. None of the figures.
	because the applicant failed to suggest a figure.
	because this figure better characterizes the invention.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-13
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

International application No. PCT/US98/08716

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The old Abstract included a Title, which is now deleted.

#### **NEW ABSTRACT**

An enriched population of mammalian dorsal neural progenitor cells, e.g., dopaminergic neural precursor cells, are described that are useful to induce neuronal regeneration in mammals suffering from a neurodegenerative disease.



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` ` '				
	According to International Patent Classification (IPC) or to both national classification and IPC			
	DS SEARCHED			
Minimum do	ocumentation searched (classification system followed	d by classification symbols)		
U.S. : 4	435/325, 368, 377			
Documentati	ion searched other than minimum documentation to the	extent that such documents are included	in the fields searched	
APS, BIO	ata base consulted during the international search (na SIS, MEDLINE ms: neural, precursor#, progenitor, stem, cell#, human			
c. Doc	UMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.	
$ \mathbf{x} $	US 5,411,883 A (BOSS et al) 02 May	1995, columns 3, 7, 11-13,	1-9	
	17 and 19-20.		10.12	
Y			10-13	
$ _{\mathbf{X}}$	US 5,589,376 A (ANDERSON et al)	31 December 1996, columns	1	
	3-4, 8-9, 11, 13-14 and 16-17.			
A	2-13			
X .	MOYER et al. Culture, Expansion, and Transplantation of Human Fetal Neural Progenitor Cells. Transplantation Proceedings. June 1997, Vol. 29, No. 4, pages 2040-2041, see entire document.			
X	US 5,656,481 A (BAETGE et al) 12 A 46-57.	august 1997, column 30, lines	1, 11-13	
Further documents are listed in the continuation of Box C. See patent family annex.				
*A* do	Special categories of cited documents     T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention.			
	to be of particular relevance  *E* earlier document published on or after the international filing date  *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step			
cit	*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other			
•0• do	considered to involve an inventive step when the document is			
	*P* document published prior to the international filing date but later than *&* document member of the same patent family the priority date claimed			
	actual completion of the international search	Date of mailing of the international se	arch report	
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230  Authorized officer  ROBERT C. HAYES, PH.D.  Telephone No. (703) 308-0196				

International application No. PCT/US98/08716

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-13, drawn to a population of mammalian neural precursor cells committed to a cell fate.

Group II, claim(s) 14-16, drawn to a method of stimulating proliferation of a heterogenous population of neural cell precursor cells to enrich for dorsal neural cells.

Group III, claim(s) 17-18 and 20, drawn to a method of inducing neuronal regeneration in an adult mammal comprising transplanting dorsal neural precursor cells.

Group IV, claim(s) 19, drawn to a method of inducing neuronal regeneration in an adult mammal comprising administering a Wnt polypeptide or Wnt agonist.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I is directed to a population of mammalian neural precursor cells, which is the first product. However, because Boss et al teach an enriched population of porcine or human neuron progenitor cells (i.e., mammalian neural precursor cells), no special technical feature exists for Group I as defined by PCT RULE 13.2, because it does not define a contribution over the prior art. The technical features of Groups II-IV are drawn to methods having different goals, method steps and starting materials, which do not share the same or a corresponding technical feature. Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Because the technical feature of Group I is not a special technical feature, and because the technical features of the Group II-IV inventions are not present in the Group I claims, unity of invention is lacking.

# CHAPTER I PCT TELEPHONE MEMORANDUM FOR LACK OF UNITY OF INVENTION

09/674292 526 Rec'd PCT/FTD 300CT 2000



PCT No.: PCT/US98/08716

Examiner: ROBERT C. HAYES, PH.D.

Attorney spoken to: JOHN FREEMAN

Date of call: 23 JULY 1998

	Amount of payment approved:
	Deposit account number to be charged:
	Attorney elected to pay for ALL additional inventions
	Attorney elected to pay only for the additional inventions covered by
	☐ Group(s):
(	encompassing
	☐ Claim(s):
☒	Attorney elected NOT to pay for any additional inventions, therefore, only the first claimed invention (Group I) covered by Claim(s) 1-13 has been searched.
×	Attorney was orally advised that there is no right to protest for any group not paid for.
×	Attorney was orally advised that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/ISA/210).

#### Time Limit For Filing A Protest

Applicant is hereby given 15 days from the mailing date of this Search Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 40.2, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

#### Detailed Reasons For Holding Lack Of Unity Of Invention:

#### Detailed Reasons For Holding Lack of Unity Of Invention:

(Continued on a separate sheet)

Note: A copy of this form must be attached to the Search Report.

# ATTACHMENT TO CHAPTER I PCT TELEPHONE MEMORANDUM FOR LACK OF UNITY OF INVENTION

#### Detailed Reasons For Holding Lack Of Unity Of Invention:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

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### **PCT**

## WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



(51) International Patent Classification <sup>6</sup> :		(11) International Publication Number: WO 99/57248		
C12N 5/06, 5/08	A1	(43) International Publication Date: 11 November 1999 (11.11.99		
21) International Application Number: PCT/USc  22) International Filing Date: 30 April 1998 (3)		CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL		
71) Applicant (for all designated States except US): PRE AND FELLOWS OF HARVARD COLLEGE [US Quincy Street, Cambridge, MA 02138 (US).				
72) Inventors; and 75) Inventors/Applicants (for US only): McMAHON, Ai [GB/US]; 128 Kendall Road, Lexington, MA 021 LEE, Scott, K. [US/US]; 54 Chestnut Street, Ca MA 02139 (US). TAKADA, Shinji [-/-]; -	173 (US	.		
74) Agent: FREEMAN, John, W.; Fish & Richardson I Franklin Street, Boston, MA 02110-2804 (US).	P.C., 2			
54) Title: INDUCTION OF NEURONAL REGENERAT	NOL			
57) Abstract				
An enriched population of mammalian dorsal neural aseful to induce neuronal regeneration in mammals suffering		or cells, e.g., dopaminergic neural precursor cells, are described that are a neurodegenerative disease.		

#### FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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EE	Estonia	LR	Liberia	SG	Singapore		

Form PCT/ISA/210 (second sheet) luly 1992)+

		<u>.                                    </u>		
A. CLASSIFICATION OF SUBJECT MATTER  IPC(6) : C12N 5/06, 5/08  US CL ::435/325, 368, 377  According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIEI	.DS SEARCHED			
Minimum d	locumentation searched (classification system followers	ed by classification symbols)		
U.S. :	435/325, 368, 377			
Documenta	tion searched other than minimum documentation to th	re extent that such documents are included	in the fields searched	
Electronic o	data base consulted during the international search (n	ame of data base and, where practicable	, search terms used)	
	osis, MEDLINE ms: neural, precursor#, progenitor, stem, cell#, huma	n, porcine, wnt#, dorsal, hippocam##, hi	ndbrain, dopamin?	
C. DOC	UMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where ap	opropriate, of the relevant passages	Relevant to claim No.	
X	US 5,411,883 A (BOSS et al) 02 May	y 1995, columns 3, 7, 11-13,	1-9	
Y	17 and 19-20.	į	10-13	
1		•	10-13	
X	US 5,589,376 A (ANDERSON et al)	31 December 1996, columns	1	
Α	3-4, 8-9, 11, 13-14 and 16-17.		2-13	
A			2-13	
X	MOYER et al. Culture, Expansion, and Transplantation of Human Fetal Neural Progenitor Cells. Transplantation Proceedings. June 1997, Vol. 29, No. 4, pages 2040-2041, see entire document.			
X	US 5,656,481 A (BAETGE et al) 12 August 1997, column 30, lines 1, 11-13 46-57.			
Furth	er documents are listed in the continuation of Box C	See patent family annex.		
* Special categories of cited documents				
	cument defining the general state of the art which is not considered one of particular relevance	date and not in conflict with the appl the principle or theory underlying the		
	her document published on or after the international filing date	"X" document of particular relevance, the considered novel or cannot be considered.		
	nument which may throw doubts on priority claim(s) or which is do to establish the publication date of another citation or other	when the document is taken alone		
spe	cial reason (as specified)	*Y* document of particular relevance, the considered ω involve an inventive considered with our process other tweethers.	step when the document is	
means being obvious to a person skilled in the art				
	*P* document published prior to the international filing date but later than "&" document member of the same patent family the priority date claimed			
Date of the	actual completion of the international search	Date of mailing of the international sea	rch report	
30 JULY	30 ЛЛLY 1998 <b>31 AUG 1998</b>			
Commission Box PCT	nating address of the ISA/US ner of Patents and Trademarks i, D.C. 20231	Authorized officer  ROBERT C. HAYES, PH.D.	John	
Facsimile No. (703) 305-3230		Telephone No. (703) 308-0196	· 10	

Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-13
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

International application No. PCT/US98/08716

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

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